Health Effects of Acid Aerosols on North American Children: Pulmonary Function

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We examined the health effects of exposure to acidic air pollution among children living in 24 communities in the United States and Canada. Parents of children between the ages of 8 and 12 completed a self-administered questionnaire and provided consent for their child to perform a standardized forced expiratory maneuver at school in 22 of these communities. Air quality and meteorology were measured in each community for the year preceding the pulmonary function tests. Forced vital capacity (FVC) and forced expiratory volume in 1 sec ($FEV_{1.0}$) measurements of 10,251 white children were examined in a two-stage regression analysis that adjusted for age, sex, height, weight, and sex–height interaction. In this study, a 52 nmol/m^3 difference in annual mean particle strong acidity was associated with a 3.5% (95% CI, 2.0–4.9) decrement in adjusted FVC and a 3.1% (95% CI, 1.6–4.6) decrement in adjusted $FEV_{1.0}$. The FVC decrement was larger, although not significantly different, for children who were lifelong residents of their communities (4.1%, 95% CI, 2.5–5.8). The relative odds for low lung function (that is, measured FVC less than or equal to 85% of predicted), was 2.5 (95% CI, 1.8–3.6) across the range of particle strong acidity exposures. These data suggest that long-term exposure to ambient particle strong acidity may have a deleterious effect on lung growth, development, and function. *Key words*: acid aerosols, air pollution, children, pulmonary function. *Environ Health Perspect* 104:506–514 (1996)

Experimental studies of sulfur dioxide and particulate pollutants have indicated adverse health effects in both animals (*1*) and human subjects (*2*). Epidemiologic studies of acute health effects have found decreased lung function (*3*), increased respiratory symptoms and illnesses (*4*), increased hospitalizations (*5,6*), and increased mortality (*7*) to be associated with current levels of particulate air pollution in many urban areas. Particle strong acidity is found in the fine-size fractions of suspended particulates, raising the possibility that the observed chronic health effects associated with respirable particulate pollution may be attributable at least in part to the acidity of the particles (*8,9*). However, previous population-based studies lacked direct measures of particle acidity; investigators used surrogate measurements to assess the possible effects of particle acidity on health. Improvements in atmospheric monitoring have resulted in the direct measurement of particle acidity in various locations throughout North America (*10*). Because of the widespread distribution of the exposure and the toxicological and clinical data suggesting potential effects, concern has been raised regarding the possible adverse health effects resulting from exposures to particle acidity (*11,12*).

Previous population-based studies have relied on measurements of pollutants that were only indirectly related to particle acidity. The Harvard Six Cities Study of 5422 children demonstrated that particulate matter <15 μm in diameter was associated with reported bronchitis in the past year, but no statistically significant associations were observed for pulmonary function (*13,14*). A later analysis suggested that the annual mean of particle strong acidity was associated with reported bronchitis in the past year [odds ratio (OR) = 2.4, 95% confidence interval (CI), 1.9–3.2] among a separate cohort of 12,302 children in these six communities plus Charleston, West Virginia (*15*), but the measurements of particle acidity were made after the collection of the health data. Authors of earlier studies suggested that the power of an epidemiologic study to detect the health effects of particle acidity would be enhanced by increasing the number of communities (*16*) and by selecting communities at the extremes of the continental scale range of aerosol acidity exposures (*17*). The present study (*18*) was specifically designed to examine the adverse health effects resulting from repeated intermittent, long-term exposures to directly measured particle strong acidity on pulmonary function and respiratory symptoms [reported in an accompanying paper (*19*)] of schoolchildren.

Methods

Air monitoring. We selected 24 communities on the basis of previously measured sulfate and ozone concentrations and demographic characteristics (*20*). We included 18 sites in the United States and 6 sites in Canada to provide a wide range of expected acid aerosol and ozone levels. Communities were predominantly suburban or rural with homogeneous, relatively stable populations and no major local sources of air pollution. Each site was monitored for approximately 12 months, and pulmonary function tests were conducted at the end of the year in all but two of the communities. Eight sites were monitored during the first year, nine sites in the second year, and seven sites in the third year of the study.

Air pollution measurement methods and results are described in an accompanying paper (*20*). We sampled particulate pollutants for 24 hr every other day for at least 11 months. Inhalable particulate matter with an aerodynamic diameter <10 μm (PM_{10}) was sampled using a Harvard Impactor (*21*). Fine particulate matter with an aerodynamic diameter >2.1 μm ($PM_{2.1}$) was sampled using a glass impactor/filter pack system. Fine particle strong acidity, fine particle sulfate, and gaseous acids (nitrous and nitric acids) were sampled using the Harvard EPA Annular Denuder System (HEADS) in 21 communities

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(*22,23*). In three communities with low levels of gas-phase acidity, the simpler Harvard Impactors with ammonia denuders were used. Strong acidity was measured by pH analysis (*24*) and sulfate by ion chromatography of the extracted particles. Ozone was monitored continuously.

Respiratory health questionnaire. In communities with fewer than 750 children enrolled in the fourth and fifth grades of public schools, all schools were included in the study. In larger communities, schools were selected according to their proximity to the air monitoring sites or randomly, depending on geography of school district(s). A standard respiratory health questionnaire was distributed to each child for completion by a parent or guardian. All questionnaires were distributed in late September or early October. A return rate of more than 90% was attained for all but six communities, where the return rate was 84% or higher (*25*). The association between particle acidity and respiratory symptoms is reported elsewhere (*25*).

Lung function testing. Pulmonary function tests were administered by trained field technicians between October and May to those children with parental permission. Pulmonary function measurements were generally scheduled in each community to be completed with the end of the air monitoring sampling. The study protocol and methods were approved by the human subjects committee at the Harvard School of Public Health and separately by local health authorities and school boards in each community. The local school boards in two communities subsequently withdrew their permission to conduct the pulmonary function testing, although questionnire data were collected.

The same centrally trained technicians administered a standard forced expiratory test throughout the study according to methods suggested by the American Thoracic Society (*26*) using a Spiroflow rolling seal spirometer system (PK Morgan, Andover, Massachusetts). All spirometers were calibrated each morning and afternoon on test days using a 3.0-l syringe and independently audited annually (*27*). Measurements were corrected to body temperature and pressure saturated with water (BTPS). Before testing, each child was asked a series of questions regarding present respiratory health, asthma and medication use, smoking habits, and recent exercise. After measurement of height and weight with shoes removed, each child performed at least five but not more than eight forced expiratory maneuvers while sitting with free mobility and with a noseclip to obtain three acceptable maneuvers. Using a computer-assisted quantitative assessment, field technicians determined the acceptability of each maneuver according to the following criteria: the blow was a good effort with a maximal inspiration, a strong start, and continuous exhalation; the back-extrapolated volume was >100 ml or 5% of forced vital capacity (FVC); the exhalation had a duration of at least 3 sec; and the change in volume in the last 2 sec was less than 45 ml. Acceptable tests were considered to be reproducible if they had an FVC and an forced expiratory flow at 1 sec ($FEV_{1.0}$) within 5% of the maximum value on an acceptable test. During the first year of the study, children enrolled in the fifth grade also performed partial flow-volume maneuvers after the full forced expiratory test (*28*).

Statistical methods. Previously reported analyses of city-specific health outcomes demonstrated a larger between-city variation than would be predicted by interindividual variation (*13,14*). In the present study, a two-step analysis was used to correct for any excess between-city variability. In the first step, we calculated city-specific adjusted means by regressing the natural logarithm of the pulmonary function measurement on sex, ln age, ln height, ln weight, and an interaction term of sex and ln height. In the second step, we regressed these adjusted means against the city-specific annual mean air pollution concentrations using weights inversely proportional to the sum of the between-city and within-city variances of the adjusted means. Analyses were done using SAS software (SAS Institute, Inc., Cary, North Carolina). Results of the weighted regression coefficients and standard errors are summarized as the estimated relative changes in pulmonary function parameters scaled to the range in the city-specific annual mean of air pollution. Stratified and sensitive subgroup analyses were conducted in a similar fashion using the two-step approach.

A second analysis assessed the prevalence of children whose pulmonary function was less than 85% of the value predicted by the analysis performed in stage one. We calculated city-specific logits of the fraction of children with FVCs <85% of predicted. The stage-two analysis was conducted as described above, but using the sum of the between-city and within-city variances of the adjusted logits as the weights. The logistic regression coefficients and their standard errors are expressed as odds ratios scaled to the range in the city-specific annual means of air pollution.

Results

A total of 15,523 questionnaires were returned, of which 14,103 had complete

Table 1. Distribution of covariates in pulmonary function model by community: 10,251 children, 22 communities, United States and Canada, 1988–1991

		No. of children			Mean		
Community	Code	Excluded	Included	%Female	Age (years)	Height (cm)	Weight (kg)
Sulfate Belt							
Hendersonville, TN	HEN	58	433	55	9.6	143.0	86.2
Oak Ridge, TN	OAK	37	487	46	9.7	141.7	82.7
Morehead, KY	MOR	61	303	49	9.7	142.4	90.5
Blacksburg, VA	BLB	100	549	46	9.5	142.2	84.3
Charlottesville, VA	CHV	96	405	45	9.5	141.4	87.2
Zanesville, OH	ZAN	103	513	49	9.7	141.9	85.1
Parsons, WV	PAR	78	478	49	9.7	141.5	86.2
Uniontown, PA	UNT	102	454	46	9.7	142.4	85.4
Penn Hill, PA	PEN	58	497	49	9.5	140.1	80.6
State College, PA	STC	58	537	50	9.5	140.4	80.2
Transport Region							
Leamington, ON	LEM	116	456	51	9.4	139.5	81.0
Newtown, CT	NEW	161	291	51	9.5	141.1	79.4
Egbert, ON	EGB	83	527	48	9.3	142.2	81.8
Pembroke, ON	PMB	92	424	48	9.4	140.4	81.0
Dunnville, ON	DUN	45	391	50	9.4	139.8	79.8
West Coast							
Simi Valley, CA	SIM	105	422	46	9.6	142.5	82.5
Livermore, CA	LIV	70	497	52	9.5	143.1	82.8
Monterey, CA	MTY	83	539	52	9.6	143.4	85.5
Background							
Springdale, AR	SPG	83	407	53	9.6	142.1	85.1
Aberdeen, SD	ABD	68	583	50	9.8	143.8	86.9
Yorkton, SK	YOR	71	542	49	9.4	141.3	82.3
Penticton, BC	PCT	94	516	46	9.4	142.1	79.9
All communities		1822	10251	49	9.5	141.8	83.4

information on selected covariates for white children age 8–12 years. We excluded 736 children because of significant medical conditions unrelated to air pollution: children with a history of cystic fibrosis, chest operations, heart conditions, or who received oxygen for more than 2 weeks after birth or at home. A total of 1537 children did not attempt the pulmonary function test, mainly due to lack of parental permission. In addition, 82 children were excluded who smoked more than five cigarettes in their lifetime, 10 children with missing heights or weights, 133 children (1%) with extreme heights (<120 cm or > 160 cm), and 133 children (1%) with extreme weights (<50 lbs or >150 lbs). After eight attempts, 721 children (6%) had no acceptable pulmonary function test, and an additional 502 children (5%) failed to have two acceptable tests. These restrictions left a data set of 10,251 children in 22 communities with at least 2 acceptable pulmonary function tests.

The communities had similar means for gender, age, height, and weight as well as similar numbers of children excluded from the analysis with the exception of Newtown, Connecticut (Table 1). Newtown was the first community examined, and a technical error led to a higher exclusion rate. Due to the restrictions on height and weight, the children were of similar stature across the 22 communities, with city-specific means ranging from 140 to 144 cm for height and from 79 to 91 lbs for weight (36–41 kg). The communities also had similar proportions of children in subgroups considered potentially sensitive to air pollutant health effects (Table 2). Approximately three-fourths of the children had lived in their current community since at least age 6, and most had lived in their current community since birth. The proportion of children in each community who were exposed to environmental tobacco smoke in the home ranged from 28% to 63%.

The ranges in the city-specific annual means (Table 3) for particulate pollutants were 51.9 nmol/m^3 for particle strong acidity, 6.8 µg/m^3 for sulfate particles, 14.9 µg/m^3 for respirable particulate matter ($PM_{2.1}$), and 17.3 µg/m^3 for inhalable particulate matter (PM_{10}). City-specific mean particle strong acidity was moderately correlated with PM_{10} [Pearson's correlation coefficient (r) = 0.47], strongly correlated with sulfate (r = 0.90) and $PM_{2.1}$ (r = 0.82), and essentially uncorrelated with gaseous acids (r = 0.07). Three exposure parameters were considered for the annual mean ozone concentration: the average maximum 1-hr mean, the average daytime 8-hr (1000–1800 hr local time) mean, and the average daily 24-hr mean. All three ozone parameters were highly correlated across the 24 communities, with Pearson correlation coefficients ranging from 0.74 to 0.98. By design, city-specific mean particle strong acidity was correlated only weakly with the three ozone parameters; the strongest correlation was with the average 1-hr maximum ozone concentration (r = 0.37). A more complete description of air monitoring results can be found in an accompanying article (*20*).

We calculated city-specific mean pulmonary function values adjusted for sex,

Table 2. Percentages of children with selected characteristics by community: 10,251 children, 22 communities, United States and Canada, 1989–1991

Community	Lifetime residents	Moved into community after 1st grade	Severe chest illness before age 2	Current smoking in the home	Maternal smoking during pregnancy	Parental asthma
Sulfate Belt						
Hendersonville, TN	38	36	13	54	26	14
Oak Ridge, TN	35	39	19	41	24	17
Morehead, KY	59	20	7	61	30	14
Blacksburg, VA	42	32	16	36	21	15
Charlottesville, VA	55	26	10	52	24	13
Zanesville, OH	70	15	17	58	31	17
Parsons, WV	65	17	18	55	30	14
Uniontown, PA	68	17	13	60	30	13
Penn Hill, PA	62	20	13	45	27	12
State College, PA	40	29	14	28	13	16
Transport Region						
Leamington, ON	69	19	14	56	24	9
Newtown, CT	44	27	13	37	23	16
Egbert, ON	40	30	18	63	37	15
Pembroke, ON	62	18	17	62	37	9
Dunnville, ON	63	20	17	58	32	14
West Coast						
Simi Valley, CA	40	32	13	40	24	18
Livermore, CA	46	28	12	34	19	19
Monterey, CA	49	28	10	30	15	18
Background						
Springdale, AR	49	27	21	61	34	14
Aberdeen, SD	59	18	20	49	26	10
Yorkton, SK	61	16	18	57	36	11
Penticton, BC	37	35	15	51	31	14
All communities	52	25	15	49	27	14

Table 3. Summary of city-specific annual mean air pollutant concentrations: 24 communities, United States and Canada, 1988–1991

Pollutant	Grand mean	SD	Minimum	Maximum	Range
Particulate matter					
Inhalable particulate matter (µg/m^3)	23.8	5.0	15.4	32.7	17.3
Respirable particulate matter (µg/m^3)	14.5	4.2	5.8	20.7	14.9
Sulfate particles (µg/m^3)[a]	4.7	2.2	0.7	7.4	6.8
Particle strong acidity (nmol/m^3)	27.5	16.2	0.0	51.9	51.9
Gaseous pollutants					
Ozone, 1-hr max (ppb)	46.5	8.5	26.9	72.5	45.6
Ozone, 8-hr daytime avg (ppb)	38.4	7.5	21.0	60.4	39.4
Ozone, 24-hr avg (ppb)	27.8	5.1	16.3	34.8	18.5
Sulfur dioxide (ppb)[b]	4.8	3.5	0.2	12.9	12.7
Ammonia (ppb)[b]	1.3	1.4	0.1	5.8	5.7
Nitrous acid (ppb)[b,c]	0.6	0.4	0.1	1.4	1.3
Nitric acid (ppb)[b,c]	0.9	0.4	0.3	2.1	2.7
Acidity					
Particle strong acidity (nmol/m^3)[b]	31.1	14.0	8.5	51.9	43.4
Gaseous acids (nmol/m^3)[b,d]	59.4	28.4	22.7	134.0	111.3
Total (nmol/m^3)[b]	90.6	33.9	38.0	150.5	112.5

[a]1 µg/m^3 = 10.4 nmol/m^3.
[b]Excluding Egbert, Ontario; Yorkton, Saskatchewan; and Aberdeen, South Dakota.
[c]1 ppb = 40.9 nmol/m^3.
[d]Gaseous acids = nitrous and nitric acid.

Table 4. Adjusted pulmonary function means and proportion of children with an FVC less than 85% of predicted by community: 10,251 children, 22 communities, United States and Canada, 1988–1991[a]

Community	FVC (l)	$FEV_{1.0}$ (l)	$FEV_{0.75}$ (l)	$FEF_{25-75\%}$ (l/sec)	PEFR (l/sec)	Proportion with FVC < 85% of predicted (%)
Sulfate Belt						
Hendersonville, TN	2.43	2.10	1.93	2.32	4.59	7.6
Oak Ridge, TN	2.41	2.06	1.90	2.19	4.54	7.6
Morehead,KY	2.42	2.06	1.89	2.21	4.38	4.6
Blacksburg, VA	2.45	2.09	1.92	2.25	4.57	6.6
Charlottesville, VA	2.38	2.06	1.90	2.25	4.55	8.9
Zanesville, OH	2.44	2.10	1.93	2.30	4.43	7.6
Parsons, WV	2.41	2.07	1.90	2.21	4.48	8.2
Uniontown, PA	2.46	2.12	1.94	2.33	4.38	6.2
Penn Hill, PA	2.45	2.11	1.95	2.35	4.59	6.0
State College, PA	2.46	2.11	1.94	2.31	4.74	5.2
Transport Region						
Leamington, ON	2.46	2.11	1.95	2.31	4.68	5.3
Newtown, CT	2.50	2.14	1.96	2.23	4.60	4.1
Egbert, ON	2.48	2.12	1.95	2.27	4.65	3.2
Pembroke, ON	2.48	2.14	1.96	2.38	4.30	3.5
Dunnville, ON	2.49	2.15	1.97	2.34	4.63	3.3
West Coast						
Simi Valley, CA	2.45	2.11	1.94	2.33	4.72	6.9
Livermore, CA	2.50	2.15	1.98	2.38	4.68	4.2
Monterey, CA	2.46	2.10	1.93	2.27	4.59	4.1
Background						
Springdale, AR	2.47	2.11	1.93	2.26	4.39	3.7
Aberdeen, SD	2.49	2.14	1.96	2.32	4.67	3.9
Yorkton, SK	2.52	2.17	1.99	2.39	4.70	2.0
Penticton, BC	2.52	2.14	1.97	2.30	4.63	3.5

Abbreviations: FVC, forced vital capacity; FEV, forced expiratory volume (1.0 = in 1 sec; 0.75 = in three-quarters second); $FEF_{25-75\%}$, forced expiratory flow between 25 and 75% FVC; PEFR, peak expiratory flow.
[a]Adjusted for age, sex, weight, height, and the interaction of sex and height.

Table 5. Percent decrement in city-specific adjusted pulmonary function measurements associated with the range of city-specific annual means of particulate pollutants: 10,251 children, 22 communities, United States and Canada, 1988-1991[a]

Pulmonary measurement	Particle strong acidity (52 nomol/m^3)	Sulfate particles (6.8 µg/m^3)	$PM_{2.1}$ (14.9 µg/m^3)	PM_{10} (17.3 µg/m^3)
FVC	-3.45 (-4.87, -2.01)[b]	-3.06 (-4.50, -1.59)	-3.21 (-4.98, -1.41)	-2.42 (-4.30, -0.51)
$FEV_{1.0}$	-3.11 (-4.62, -1.58)	-2.63 (-4.18, -1.05)	-2.81 (-4.66, -0.94)	-2.09 (-4.00, -0.14)
$FEV_{0.75}$	-3.02 (-4.49, -1.53)	-2.53 (-4.05, -1.00)	-2.72 (-4.52, -0.88)	-1.98 (-3.85, -0.07)
$FEF_{25-75\%}$	-3.47 (-6-54, -0.29)	-2.87 (-5.87, 0.23)	-2.73 (-6.28, 0.95)	-1.28 (-4.85, 2.43)
PEFR	-3.71 (-7.10, -0.20)	-2.85 (-6.21, 0.63)	-3.28 (-7.11, 0.71)	-2.03 (-5.85, 1.95)
$FEV_{1.0}$/FVC	0.36 (-0.32, 1.04)	0.44 (-0.18, 1.10)	0.42 (-0.31, 1.16)	0.37 (-0.33, 1.07)
$FEV_{0.75}$/FVC	0.45 (-0.38, 1.27)	0.54 (-0.21, 1.30)	0.52 (-0.36, 1.41)	0.49 (-0.35, 1.33)
$FEF_{25-75\%}$/FVC	-0.01 (-2.81, 2.86)	0.19 (-2.45, 2.91)	0.51 (-2.53, 3.64)	1.20 (-1.68, 4.16)

Abbreviations: $PM_{2.1}$, respirable particulate matter; PM_{10}, inhalable particulate matter; FVC, forced vital capacity; FEV, forced expiratory volume (1.0 = in 1 sec; 0.75 = in three-quarters second); $FEF_{25-75\%}$, forced expiratory flow between 25 and 75% FVC; PEFR, peak expiratory flow.
[a]Adjusted for age, sex, weight, height, and the interaction of sex and height.
[b]Confidence intervals in parentheses.

age, height, weight, and the interaction of sex with height (Table 4). Adjusted FVC ranged from a low of 2.38 l in Charlottesville, Virginia, to a high of 2.52 l in Penticton, British Columbia, and Yorkton, Saskatchewan. The coefficients of variation for these city-specific pulmonary function values were small (range 0.4–0.6% for FVC) because of the narrow age range of the children studied in each community. The city-specific adjusted means of the five pulmonary function parameters were highly correlated, with Pearson correlation coefficients ranging from 0.99 for the association of $FEV_{1.0}$ with forced expiratory volume at three-quarters of a second ($FEV_{0.75}$) to 0.50 for the association of forced expiratory flow between 25% and 75% of FVC ($FEF_{25-75\%}$) with peak expiratory flow rate (PEFR). The ratio of $FEV_{1.0}$ and FVC was only weakly correlated with the basic pulmonary function measurements across the 22 communities, with the strongest correlation shown for $FEF_{25-75\%}$ (r = 0.37). The proportion of children with an FVC <85% of predicted ranged from 2.0% in Yorkton, Saskatchewan to 8.9% in Charlottesville, Virginia.

Particulate air pollutants, including measurements of particle strong acidity, were associated with decreased pulmonary function levels among the children in these communities (Table 5). Particle strong acidity across the 22 communities (range 52 nmol/m^3) was associated with a 3.5% decrement (95% CI, -4.9 to -2.0) in FVC (Fig. 1). Controlling for daytime ozone had little effect on the association between FVC and particle strong acidity (Fig. 1). Similar differences in FVC were seen for the other particulate pollutants (Table 5), with the smallest decrement in FVC (-2.4%, 95% CI, -4.3 to -0.5) associated with the 17.3 µg/m^3 range in PM_{10} concentrations. The other measures of pulmonary function, including $FEF_{25-75\%}$ and PEFR, showed decrements similar to that for FVC. The ratios of the pulmonary function measurements with FVC were not associated with any of the measured air pollutants.

All three ozone parameters were associated with a decrease in pulmonary function (Table 6); daytime mean ozone showed the strongest association (Fig. 2). Although the association with daytime mean ozone alone was statistically significant (-3.7% difference in FVC scaled to the range of 39.4 ppb in daytime ozone), adding particle strong acidity into the model (Fig. 2) resulted in a substantial attenuation of the daytime ozone effect (-2.2%, 95% CI, -4.2 to -0.2, difference in FVC scaled to the range of daytime mean ozone). This suggests that the association between daytime ozone and adjusted FVC is partially explained by the correlation of daytime mean ozone with particle strong acidity. However, the explained variation in FVC associated with particle strong acidity was independent of daytime mean ozone (Fig. 1).

Stratification of the sample population did not greatly affect the association of adjusted FVC with particle strong acidity (Fig. 3). No differences in the association were observed with regard to geography, year of study, gender, or exercise before the pulmonary function test. Children who lived in the community at least since the age of 2 had a stronger association between

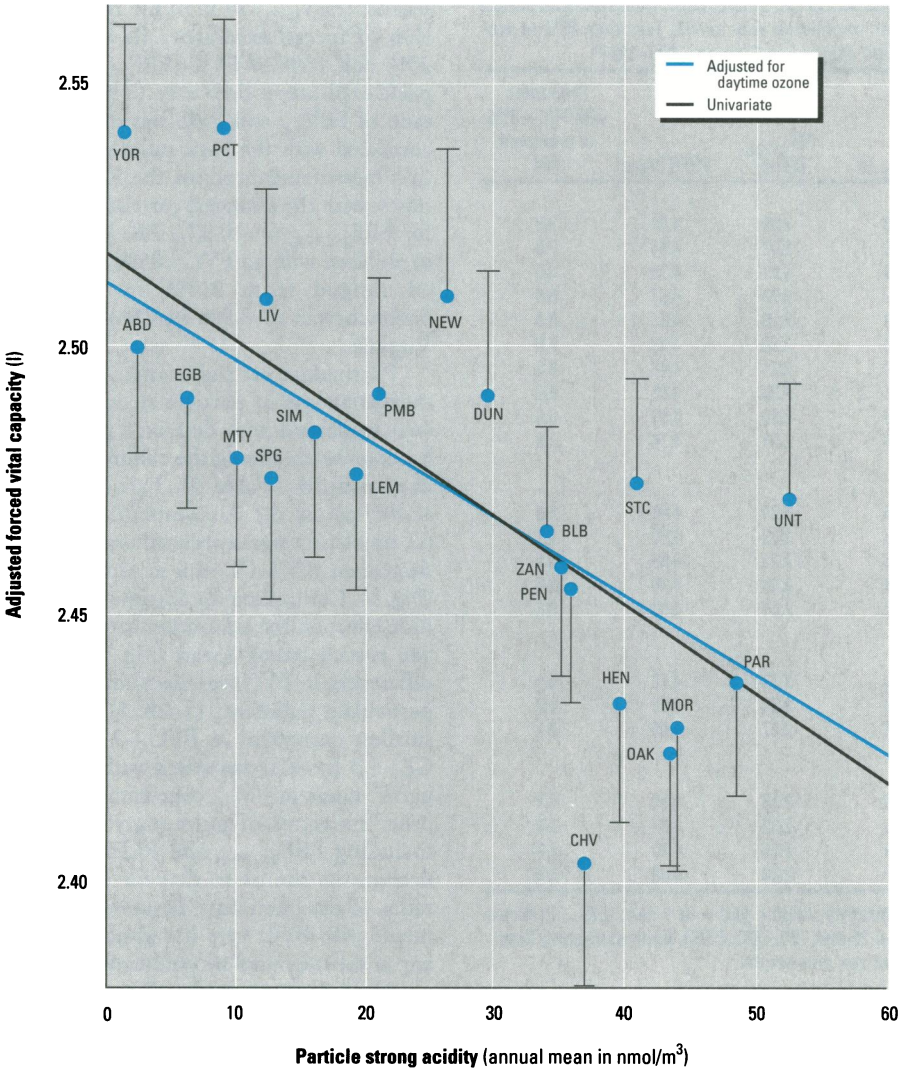

Figure 1. Association of forced vital capacity (FVC) with particle strong acidity adjusted for age, height, weight, sex, and the interaction between sex and height: 22 cities, United States and Canada, 1988–1991. One-half 95% confidence intervals for each city-specific FVC mean are shown. Site codes are provided in Table 1.

Table 6. Percent decrement in city-specific adjusted pulmonary function measurements associated with the range of city-specific annual means of ozone parameters: 10,251 children, 22 communities, United States and Canada, 1988–1991[a]

Pulmonary measurement	24-hr ozone (18.5 ppb)	Daytime ozone (39.4 ppb)	1-hr max ozone (45.6 ppb)
FVC	-2.87 (-4.82,-0.88)[b]	-3.74 (-6.45, -0.94)	-3.57 (-6.39, -0.67)
$FEV_{1.0}$	-2.93 (-4.80, -1.02)	-3.55 (-6.24, -0.78)	-3.29 (-6.10, -0.39)
$FEV_{0.75}$	-2.84 (-4.66, -0.98)	-3.23 (-5.91, -0.47)	-2.94 (-5.74, -0.06)
$FEF_{25-75\%}$	-4.00 (-7.35, -0.53)	-3.98 (-8.89, 1.20)	-3.49 (-8.58, 1.89)
PEFR	-0.52 (-4.80, 3.96)	0.96 (-5.00, 7.29)	1.07 (-4.99, 7.50)
$FEV_{1.0}$/FVC	-0.06 (-0.84, 0.72)	0.20 (-0.87, 1.29)	0.32 (-0.77, 1.41)
$FEV_{0.75}$/FVC	0.03 (-0.91, 0.97)	0.54 (-0.75, 1.83)	0.68 (-0.61, 1.98)
$FEF_{25-75\%}$/FVC	-1.20 (-4.22, 1.92)	-0.25 (-4.54, 4.24)	0.14 (-4.24, 4.71)

Abbreviations: $PM_{2.1}$, respirable particulate matter; PM_{10}, inhalable particulate matter; FVC, forced vital capacity; FEV, forced expiratory volume (1.0 = in 1 sec; 0.75 = in three-quarters second); $FEF_{25-75\%}$, forced expiratory flow between 25 and 75% FVC; PEFR, peak expiratory flow.
[a]Adjusted for age, sex, weight, height, and the interaction of sex and height.
[b]Confidence intervals in parentheses.

particle strong acidity and FVC (-4.1%, 95% CI, -5.8 to -2.5) as compared to those who moved into the community after the first grade (-2.4%, 95% CI, -3.9 to -0.9).

Children whose parents reported a history of asthma had a slightly stronger association between FVC and particle strong acidity, although the confidence intervals were wide (Fig. 4). None of the subgroups showed a significant difference from the result for the entire sample. In particular, asthmatic children and children exposed to environmental tobacco smoke in the home had the same decrement in FVC as observed for the total sample.

Air pollution was associated with the children whose measured FVC was <85% of predicted (Fig. 5). Particle strong acidity across the range of exposures was associated with a nearly threefold increase in the proportion of children with an FVC <85% of predicted (OR = 2.5, 95% CI, 1.8–3.6). The association of particle strong acidity and low FVC was not altered by an adjustment for ozone. Particle strong acidity had a weaker association with an $FEV_{1.0}$ <85% of predicted (OR = 1.7, 95% CI, 1.2–2.3) and with an $FEV_{1.0}$ to FVC ratio less than 85% of predicted (OR = 1.1, 95% CI, 0.6–2.0). For ozone, the odds ratio for an FVC <85% of predicted was 2.9 (95% CI, 1.4–5.8) for the range of ozone observed in this study, but the relative odds was reduced to 2.0 (95% CI, 1.6–2.5) after controlling for the effect of particle strong acidity (Fig. 5). The spatial distribution of the prevalence of FVC <85% of predicted reveals consistently higher frequencies among the communities of the Sulfate Belt (Table 4).

Discussion

This study was designed to determine whether long-term exposure to acidic aerosols as estimated by 1 year of aerometric data was associated with observable decrements in lung function in children. The data from this study indicate that particle strong acidity across the range (52 nmol/m^3) of observed concentrations was associated with statistically significant decrements in FVC (-3.5%, 95% CI, -4.9 to -2.0) and $FEV_{1.0}$ (-3.1%, 95% CI, -4.6 to -1.6). All pulmonary function measures, including $FEF_{25-75\%}$ and PEFR, were negatively associated with particle strong acidity, $PM_{2.1}$, and sulfate, but neither the $FEV_{1.0}$/FVC ratio nor any other ratio measure of pulmonary function was associated with these pollutants. The relatively small differences in mean pulmonary function reflect more important differences in the proportion of children with pulmonary function levels <85% of the predicted value. The OR for children with an FVC <85% of

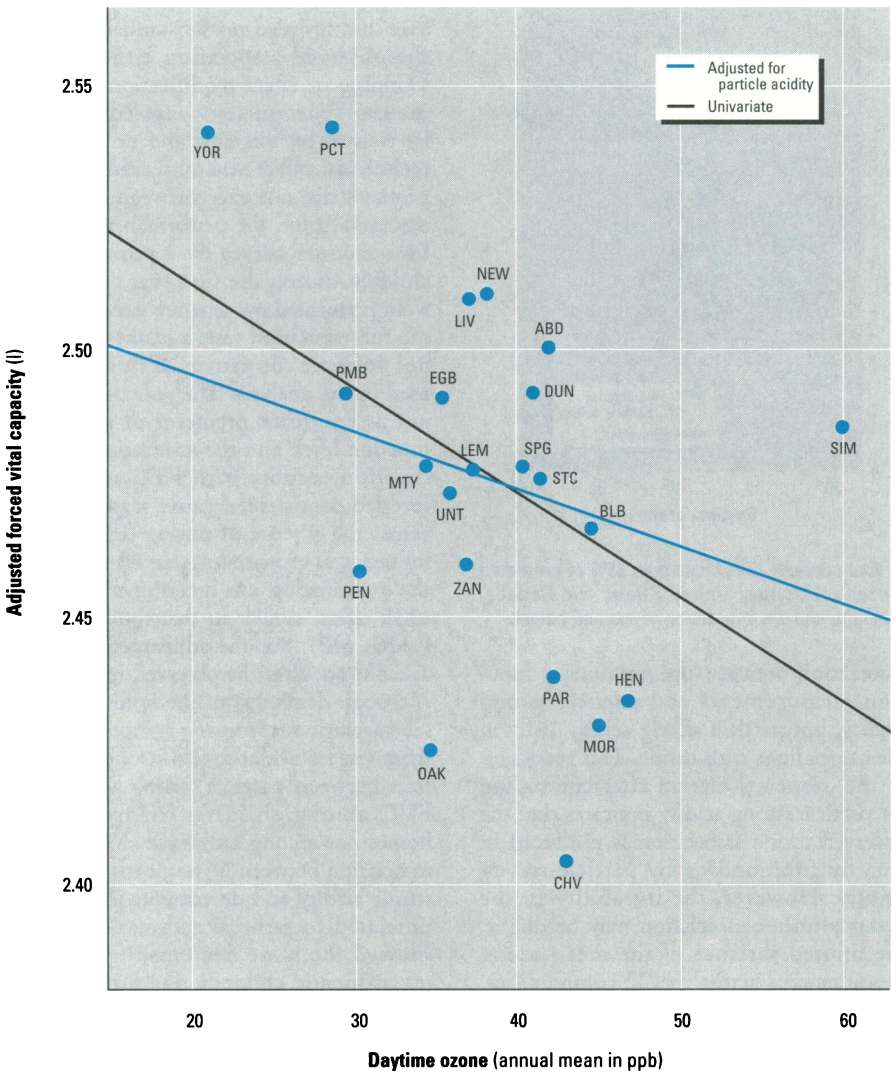

Figure 2. Association of forced vital capacity with daytime ozone adjusted for age, height, weight, sex, and the interaction between sex and height: 22 cities, United States and Canada, 1988–1991.

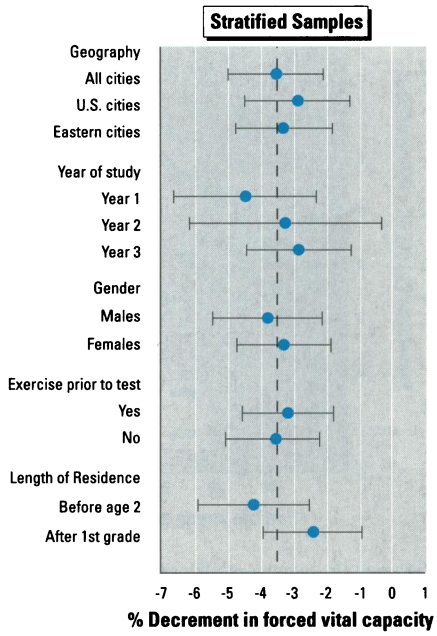

Figure 3. Percent decrement in forced vital capacity and 95% confidence intervals for a 52 nmol/m^3 increment in particle strong acidity by stratified samples of children or communities adjusted for age, height, weight, sex, and the interaction between sex and height: 22 cities, United States and Canada, 1988–1991. Dashed line indicates overall estimated effect.

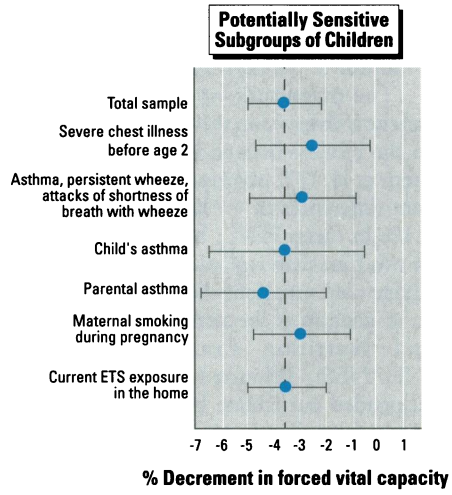

Figure 4. Percent decrement in forced vital capacity and 95% confidence intervals for a 52 nmol/m^3 increment in particle strong acidity for potentially sensitive subgroups of children adjusted for age, height, weight, sex, and the interaction between sex and height: 22 cities, United States and Canada, 1988–1991. Dashed line indicates overall estimated effect.

predicted was 2.5 (95% CI, 1.8–3.6) for the range of particle strong acidity.

Consistency with Previous Studies

Animal toxicological studies have demonstrated the additive and synergistic potential of particle strong acidity for different pulmonary endpoints. Amdur and Chen (*29*) exposed guinea pigs to varying concentrations of acidic aerosols in combination with zinc oxide and observed a dose–response relationship with bronchial reactivity. Schlesinger et al. (*30,31*) demonstrated the effects of inhaled acid sulfates on macrophage and mucocilliary clearance of particles in rabbits.

Clinical controlled exposure studies have provided evidence of adverse responses in selected subjects after acid aerosol exposure, in some cases approaching concentrations observed in ambient settings. Utell et al. (*32*) found a significant reduction in $FEV_{1.0}$ among 15 asthmatics after 20 min of exposure to 350 µg/m^3 (equivalent to 7100 nmol/m^3 of strong acidity) of a monodispersed sulfuric acid aerosol. Koenig et al. (*33*) examined the effects of acid exposures on asthmatic adolescents and demonstrated a modest decrement in lung function performance after exposure with moderate levels of exercise. Linn et al. (*34*) observed significant $FEV_{1.0}$ changes in 15 nonasthmatic subjects exposed to 2,272 µg/m^3 of a sulfuric acid aerosol with a volume median droplet diameter of 1 µm, but at levels of 122 to 410 µg/m^3 (equivalent to 2500 to 8400 nmol/m^3 of strong acidity), the changes were not statistically significant (*35*).

The acute health effects of particle acidity on young people attending summer camps have been studied, with inconsistent results. Studies by Lippman et al. (*36*), Lioy et al. (*37*), and Spektor et al. (*38*) did not reveal significant effects of acid aerosol exposures on the lung function of children. Raizenne et al. (*39*) reported that modest

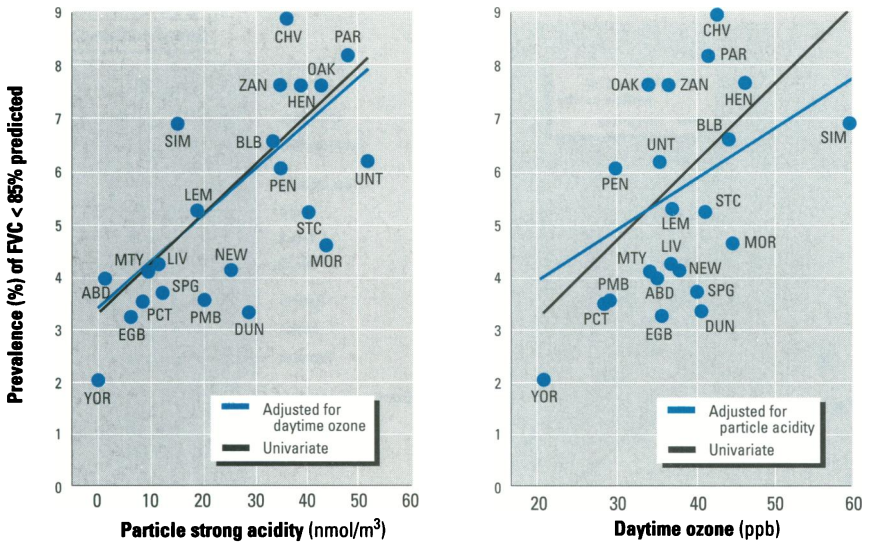

Figure 5. Prevalence of children with a measured forced vital capacity (FVC) less than 85% of predicted by annual mean particle strong acidity and daytime ozone: 22 cities, United States and Canada, 1988–1991. Predicted FVC was based on age, sex, weight, height, and the interaction of sex and height.

decrements in lung function were associated with periods of elevated particle strong acidity. Recently, Neas et al. (*40*) observed an association between elevated daytime levels of particle strong acidity with one episode exceeding 676 nmol/m^3 and decreased evening peak expiratory flow measurements (-2.5 l/min for a 12-hr exposure to a 125 nmol/m^3 increment in particle strong acidity) among 86 children in Uniontown, Pennsylvania.

The magnitude of the effect on lung function observed in this study is comparable to the results observed by other researchers. Stern et al. (*17*) observed statistically significant differences of 1.7% in mean FVC and 2.1% in mean $FEV_{1.0}$ between the children in two Canadian regions whose annual mean sulfate concentrations differed by 6.0 µg/m^3. In an analysis of the second National Health and Nutrition Examination Survey (NHANES), Schwartz (*16*) found that total suspended particulate levels across 44 geographic sampling units were associated with decrements in FVC, $FEV_{1.0}$, and PEFR among nonsmoking adults. Chestnut et al. (*41*), using data from the first NHANES, also found that exposure to total suspended particulates was associated with decrements in FVC and $FEV_{1.0}$ among nonsmoking adults living in 49 cities, but not with $FEF_{25-75\%}$ or with the $FEV_{1.0}$/FVC ratio.

Several ozone exposure metrics were used in the assessment including 8-hr daytime mean, 24-hr mean, and 1-hr maximum. For all of these parameters, the magnitudes of the associations between ozone and lung function for both FVC and $FEV_{1.0}$ were similar (Table 6). In analyses with two pollutants, ozone did not alter the association between the pulmonary function measurements and particle strong acidity, but particle strong acidity reduced the associations with ozone. This reduction in the ozone association after controlling for particle strong acidity indicates that the observed ozone association is produced in part by confounding by particle strong acidity. However, the instability in the observed ozone association may be due to the limited variance of the mean ozone measurements across the 22 communities. The present data may not be sufficiently heterogeneous to reliably assess the chronic pulmonary effects of ozone in children.

Potential Limitations

Epidemiologic studies are vulnerable to selection, information, and confounding biases. In this cross-sectional study, the observed associations with acid aerosols may be confounded by other pollutants or by other city-specific characteristics.

The site selection process provided a range of particle strong acidity exposures with little correlation with ozone exposures. The 22 communities were selected to be demographically similar to the communities in the Harvard Six Cities Study and to cover the range of exposures to particle strong acidity across the United States and Canada. No prior information on respiratory health was used in the site selection process. Across these 22 communities, the children had similar mean levels of selected covariates (Tables 1 and 2), and the effect of any differences in the distributions of sex, age, height, and weight were controlled in the first stage of the analysis by an individual level regression model.

The influence of covariates was examined and revealed no substantial effects on the observed association either as confounding or effect modification. The pulmonary function tests were administered by trained technicians, and no consistent technician effect was observed. The test protocol did not vary between communities, aside from the performance of partial flow-volume curves by a portion of the children during the first year. These tests were performed on separate occasions after the full expiration tests and thereby would not influence the pattern of data collection used in the analysis. The year of study was not a significant predictor of pulmonary function level, and the association of particle strong acidity with FVC and $FEV_{1.0}$ revealed consistent negative slope estimates across the 3 years of testing (Fig. 3). The influence of exercise less that 30 min before the examination was determined to have a small effect, similar to that found in other studies (*42*), but the adjustment for exercise did not alter the observed relationship. Although dampness of the home was associated with respiratory symptoms (*43*), there was no evidence of a stronger association between particle strong acidity and FVC among children living in damp homes nor among asthmatic children. The association between higher levels of particle strong acidity and decrements in FVC was unrelated to asthma: asthmatic children showed the same decrement in FVC as nonasthmatic children, the prevalence of an $FEV_{1.0}$ to FVC ratio <85% of predicted was not associated the particle strong acidity, and the prevalence of asthma and asthmatic symptoms was not associated with particle strong acidity among these children (*25*). The child's sex did not alter the observed response to pollution.

Chronic air pollution exposure in each community was estimated by the long-term mean concentration based on at least 11 months of monitoring. It is possible that the year of air monitoring in each community was not representative of previous years of exposure. Brook and Spengler (*44*) have reviewed available historical aerometric and meteorologic data available in several regions and have concluded that the exposure measure assigned to each community was relatively stable and that no factors were observed that altered the relative ranks of the communities for particle strong acidity, ozone, or PM_{10}. The effect of length of residence in the community was examined using the questionnaire data. More than half of the subjects had lived in their respective communities from birth, and there is some evidence that the association of particle strong acidity with FVC was greater

among those children who were lifelong residents of the communities (-4.1%, 95% CI, -2.5 to -5.8).

Personal activity and exposure patterns could have affected the lung function of individuals within each community. This effect cannot be determined within the design of the present study, but it is unlikely that there were significant activity pattern differences across the communities that would be directly correlated with annual exposures. Exposure misclassification cannot be excluded as a potential factor that could affect the magnitude of the observed association; however nondifferential misclassification of exposure would tend to bias the association towards the null hypothesis.

Particle acidity, sulfate, and fine particulate matter have a common origin in the combustion of fossil fuels and have similar long-range regional transport characteristics. Across the 22 communities in this study, particle strong acid was strongly correlated with sulfates (r = 0.90) and with $PM_{2.1}$ (r = 0.82), but less correlated with the PM_{10} measurements (r = 0.47). This correlation limits the ability to attribute the observed decreased in lung function to any particular pollutant. Measurements of particle strong acidity were slightly better predictors of a pulmonary function decrement, but these differences are not significant and may only reflect differences in the precision of the various measurement techniques as indicators of a common unmeasured or poorly measured pollutant.

The evidence of an association between fine acidic particulates and lung function may have significant health implications. Three possible explanations for a decrement in pulmonary function include submaximal inspiration to less than total lung capacity, incomplete expiration to residual volume, and reduced total lung capacity. The first hypothesis suggests that inflammation of the airways results in a child's inability to take a deep breath by either blockage of the airways or sensory inhibition stopping the child from taking a deep breath. While in adults this mechanism would tend to produce greater decrements in FVC than $FEV_{1.0}$, in children similar reductions in both measures would be anticipated, as occurred in this study. The second hypothesis suggests that peripheral airway inflammation would result in children not being able to expire to their true residual volumes due to airway closure. This was suggested by Becklake et al. (*45*) in a study that directly measured increased closing volumes among children living in a polluted city. In this case, the peripheral airway inflammation would tend to reduce the measures of flow at lower lung volumes, such as $FEF_{25-75\%}$, more than FVC measurements. This was not seen in the associations with particle strong acidity, although the ozone associations suggested such a difference. The third hypothesis would propose that the growth rate of children's lungs has been reduced with all measurements of pulmonary function level equally affected. Pulmonary function measurements obtained by this study do not permit the direct determination of each child's true total lung capacity. The essentially symmetrical reductions in FVC, $FEV_{1.0}$, $FEF_{25-75\%}$, and PEFR with no significant differences in any of the ratio measures is consistent with any of these hypotheses.

In summary, in this study we found a modest but significant reduction in pulmonary function level among children associated with living in communities with higher levels of respirable particulates, including directly measured particle strong acidity. If these children continue on this track in the growth of their lung function, as suggested by previous studies, exposure to particle acidity may put these children at a disadvantage in the future. Because of the cross-sectional nature of the current study, further studies will be necessary to determine if these outcomes are found in older children who have entered their adolescent growth phase. Whether these or other exposed children are at greater risk of both acute and chronic response to other ambient or respiratory pollutants such as occupational or personal exposures to environmental tobacco smoke or other pollutants will need to be explored.

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